MARKET WATCH

Upcoming market catalysts in Q4 2016

Potential important market catalysts in the fourth quarter of 2016 include an FDA approval decision for Heplisav (developed by Dynavax and Pfizer) for the immunization of adults against hepatitis B infection. Additionally, an FDA approval decision for telotristat etiprate (developed by Lexicon Pharmaceuticals) for neuroendocrine tumours and top-line phase III data for solanezumab (developed by Eli Lilly and PDL BioPharma) for mild Alzheimer disease (AD) are expected.

The FDA is expected to make a decision regarding the biologics license application (BLA) for Heplisav by the Prescription Drug User Fee Act (PDUFA) action date of 15 December 2016. An FDA advisory committee was originally scheduled to review the application for Heplisav on 16 November 2016; however, the FDA informed Dynavax that the meeting was cancelled and remaining questions will be addressed via the normal process. Heplisav is a prophylactic vaccine for hepatitis B based on Dynavax's proprietary immunostimulatory sequence, which specifically targets Toll-like receptor 9 to stimulate an innate immune response. Dynavax originally submitted a BLA for Heplisav to the FDA in April 2012, but the company received a complete response letter in May 2013, following a negative vote at an advisory committee meeting based on safety concerns. In the phase III HBV-23 study, which compared the safety and immunogenicity of Heplisav with the approved vaccine Engerix-B (marketed by GlaxoSmithKline), the rates of clinically adverse events, including the rate of occurrence of autoimmune disease, were consistent with results received from previous trials. The other co-primary end point of non-inferiority of seroprotection in participants with diabetes mellitus was met and the greater percentage of seroprotection provided by Heplisav compared with Engerix-B was statistically significant. If approved, Heplisav could become a major competitor for Engerix-B, given the higher seroprotection rate and the lower frequency of treatment.

Telotristat etiprate is an orally delivered small molecule designed to inhibit peripheral serotonin synthesis through the inhibition of the enzyme tryptophan hydroxylase, which

catalyses the first step of serotonin synthesis.

The FDA has granted telotristat etiprate fast-track status and orphan drug designation for the treatment of carcinoid syndrome in patients for whom the standard-of-care somastatin analogue therapy provides inadequate control. The new drug application (NDA) for telotristat etiprate was granted priority review and a PDUFA action date was set for 30 November 2016. The approval decision will be based on the phase III TELESTAR study, for which published results showed a statistically significant reduction from baseline compared with placebo for the primary end point of average number of daily bowel movements over the 12-week study period. If approved, telotristat etiprate will be a first-in-class therapy.

Eli Lilly anticipates releasing top-line data from its phase III EXPEDITION-3 study of solanezumab for mild AD in the fourth quarter of 2016. Solanezumab is a monoclonal antibody that binds to soluble monomeric forms of amyloid β , theoretically clearing it from the brain before it clumps to form amyloid plaques. Results from the phase III EXPEDITION-1 and EXPEDITION-2 studies reported in 2012 showed that solanezumab did not meet the primary cognitive and functional end points in patients with mild-to-moderate AD; however, a pre-specified secondary subgroup analysis showed a statistically significant slowing of cognitive decline in patients with mild AD. The EXPEDITION-3 study, which began in July 2013, has enrolled approximately 2,100 patients with mild AD and demonstrated brain amyloid burden. If the results confirm those seen in the subgroup analysis, this could provide a boost both for the amyloid hypothesis of AD, and for ongoing efforts to intervene earlier in the course of AD, including EXPEDITION-PRO, a phase III trial recently initiated by Lilly to study solanezumab in prodromal AD.

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*doi:10.1038/nrd.2016.186
Published online 29 Sep 2016*

The author declares no competing interests.